Frequency and Clinical Presentation of Mucocutaneous Disease Due to Mycoplasma pneumoniae Infection in Children With Community-Acquired Pneumonia

Meyer Sauteur, Patrick M ; Theiler, Martin ; Buettcher, Michael ; Seiler, Michelle ; Weibel, Lisa ; Berger, Christoph

Abstract: Importance The diagnosis of Mycoplasma pneumoniae infection as the cause of mucocutaneous disease is challenging because current diagnostic tests are not able to differentiate M pneumoniae infection from carriage. Objective To examine the frequency and clinical presentation of M pneumoniae-induced mucocutaneous disease in children with community-acquired pneumonia (CAP) using improved diagnostics. Design, Setting, and Participants This prospective, longitudinal cohort study included 152 children aged 3 to 18 years with CAP enrolled in a CAP study from May 1, 2016, to April 30, 2017, at the University Children's Hospital Zurich. Children were inpatients or outpatients with clinically defined CAP according to the British Thoracic Society guidelines. Data analysis was performed from July 10, 2017, to June 29, 2018. Main Outcomes and Measures Frequency and clinical presentation of M pneumoniae-induced mucocutaneous disease in childhood CAP. Mycoplasma pneumoniae infection was diagnosed by polymerase chain reaction (PCR) of oropharyngeal samples and confirmed with the measurement of specific peripheral blood IgM antibody-secreting cells by enzyme-linked immunospot assay to differentiate M pneumoniae-infected patients from carriers with CAP caused by other pathogens. Mucocutaneous disease was defined as any eruptive lesion that involved skin and/or mucous membranes occurring during the CAP episode. Results Among 152 enrolled children with CAP (median [interquartile range] age, 5.7 [4.3-8.9] years; 84 [55.3%] male), 44 (28.9%) tested positive for M pneumoniae by PCR; of these, 10 children (22.7%) developed mucocutaneous lesions. All 10 patients with mucocutaneous eruptions tested positive for specific IgM antibody-secreting cells. Skin manifestations were found in 3 cases (2.8%) of M pneumoniae PCR-negative CAP ($P < .001$). The spectrum of M pneumoniae-induced mucocutaneous disease included M pneumoniae-induced rash and mucositis (3 cases [6.8%]), urticaria (2 cases [4.5%]), and maculopapular skin eruptions (5 cases [11.4%]). Two patients had ocular involvement as the sole mucosal manifestation (bilateral anterior uveitis and nonpurulent conjunctivitis). Patients with M pneumoniae-induced mucocutaneous disease had longer duration of prodromal fever (median [interquartile range], 10.5 [8.3-11.8] vs 7.0 [5.5-9.5] days; $P = .02$) and higher C-reactive protein levels (median [interquartile range], 31 [22-59] vs 16 [7-23] mg/L; $P = .04$) than patients with CAP due to M pneumoniae without mucocutaneous manifestations. They were also more likely to require oxygen (5 [50%] vs 1 [5%]; $P = .007$), to require hospitalization (7 [70%] vs 4 [19%]; $P = .01$), and to develop long-term sequelae (3 [30%] vs 0; $P = .03$). Conclusions and Relevance Mucocutaneous disease occurred significantly more frequently in children with CAP due to M pneumoniae than in children with CAP of other origins. Mycoplasma pneumoniae-induced mucocutaneous disease was associated with increased systemic inflammation, morbidity, and a higher risk of long-term sequelae.

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Patrick M. Meyer Sauteur, MD, PhD; Martin Theiler, MD; Michael Buettcher, MD; Michelle Seiler, MD; Lisa Weibel, MD; Christoph Berger, MD

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OBJECTIVE To examine the frequency and clinical presentation of *M pneumoniae*–induced mucocutaneous disease in children with community-acquired pneumonia (CAP) using improved diagnostics.

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RESULTS Among 152 enrolled children with CAP (median [interquartile range] age, 5.7 [4.3-8.9] years; 84 [55.3%] male), 44 (28.9%) tested positive for *M pneumoniae* by PCR; of these, 10 children (22.7%) developed mucocutaneous lesions. All 10 patients with mucocutaneous eruptions tested positive for specific IgM antibody–secreting cells. Skin manifestations were found in 3 cases (2.8%) of *M pneumoniae* PCR-negative CAP ($P < .001$). The spectrum of *M pneumoniae*–induced mucocutaneous disease included *M pneumoniae*–induced rash and mucositis (3 cases [6.8%]), urticaria (2 cases [4.5%]), and maculopapular skin eruptions (5 cases [11.4%]). Two patients had ocular involvement as the sole mucosal manifestation (bilateral anterior uveitis and nonpurulent conjunctivitis). Patients with *M pneumoniae*–induced mucocutaneous disease had longer duration of prodromal fever (median [interquartile range], 10.5 [8.3-11.8] vs 7.0 [5.5-9.5] days; $P = .02$) and higher C-reactive protein levels (median [interquartile range], 31 [22-59] vs 16 [7-23] mg/L; $P = .04$) than patients with CAP due to *M pneumoniae* without mucocutaneous manifestations. They were also more likely to require oxygen (5 [50%] vs 1 [5%]; $P = .007$), to require hospitalization (7 [70%] vs 4 [19%]; $P = .01$), and to develop long-term sequelae (3 [30%] vs 0; $P = .03$).

CONCLUSIONS AND RELEVANCE Mucocutaneous disease occurred significantly more frequently in children with CAP due to *M pneumoniae* than in children with CAP of other origins. *Mycoplasma pneumoniae*–induced mucocutaneous disease was associated with increased systemic inflammation, morbidity, and a higher risk of long-term sequelae.

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Editorial
Supplemental content

Author Affiliations: Division of Infectious Diseases and Hospital Epidemiology, University Children's Hospital Zurich, Zurich, Switzerland (Meyer Sauteur, Berger); Division of Pediatric Dermatology, University Children's Hospital Zurich, Zurich, Switzerland (Theiler, Weibel); Dermatology Department, University Hospital Zurich, Zurich, Switzerland (Theiler, Weibel); Division of Infectious Diseases, Children's Hospital Lucerne, Lucerne, Switzerland (Buettcher); Emergency Department, University Children's Hospital Zurich, Zurich, Switzerland (Seiler).

Corresponding Author: Patrick M. Meyer Sauteur, MD, PhD, Division of Infectious Diseases and Hospital Epidemiology, University Children's Hospital Zurich, Steinwiesstrasse 75, Zurich CH-8032, Switzerland (patrick.meyer@kispi.uzh.ch).

Mycoplasma pneumoniae is a frequent cause of childhood community-acquired pneumonia (CAP).[1] In addition, *M pneumoniae* can cause extrapulmonary disease, including mucocutaneous manifestations.[2] These manifestations include maculopapular skin eruptions, urticaria, and mucocutaneous eruptions along the spectrum of erythema multiforme, Stevens-Johnson syndrome, and toxic epidermal necrolysis.[2] Mucocutaneous eruptions due to *M pneumoniae* frequently present with prominent mucositis and minimal or even absent cutaneous involvement, referred to as *M pneumoniae*-induced rash and mucositis (MIRM).[3] Diagnosis of *M pneumoniae* infection in such cases has mainly been based on serologic testing and rarely on polymerase chain reaction (PCR) of upper respiratory tract specimens.[2-4] However, PCR and serologic testing for *M pneumoniae* are not able to reliably differentiate infected patients from carriers with CAP caused by other pathogens.[5,6] *M pneumoniae* carriage in the upper respiratory tract has been reported in up to 56% of healthy children.[5-7] Thus, the detection of *M pneumoniae* with these currently available diagnostic tests may cause an overestimation of the *M pneumoniae*-induced mucocutaneous disease burden.

A recent prospective, longitudinal CAP study[6] among children found that the measurement of specific peripheral blood IgM antibody-secreting cells (ASCs) by an enzyme-linked immunospot (ELISpot) assay improved diagnosis of *M pneumoniae* infection.[6] Using this data set, we aimed to assess the frequency and clinical presentation of *M pneumoniae*-induced mucocutaneous disease in childhood CAP.

Key Points

Question What are the frequency and clinical characteristics of *Mycoplasma pneumoniae*–induced mucocutaneous disease in children with community-acquired pneumonia (CAP)?

Findings In this cohort study of 152 children with CAP, mucocutaneous eruptions developed in 10 of 44 patients (22.7%) with CAP due to *M pneumoniae* and 3 of 108 patients (2.8%) with CAP of other causes, a significant difference. Among patients with *M pneumoniae* infection, mucocutaneous disease was significantly associated with longer duration of fever, higher C-reactive protein level, and greater likelihood of hospitalization, oxygen use, and sequelae.

Meaning The findings suggest that mucocutaneous disease is a frequent manifestation of *M pneumoniae* infection in children and is associated with increased systemic inflammation, morbidity, and a higher risk of long-term sequelae.

Methods

Patients

This cohort study included patients enrolled between May 1, 2016, and April 30, 2017, at University Children's Hospital Zurich. The primary inclusion criterion was CAP defined according to the British Thoracic Society guidelines[8] in previously healthy children aged 3 to 18 years.[6] Mucocutaneous disease was defined as any eruptive lesion that involved skin and/or mucous membranes occurring during the CAP episode; MIRM was defined as involvement of 2 or more mucosal sites with absent or limited skin lesions.[3] Data analysis was performed from July 10, 2017, to June 29, 2018. The ethics committee of Zurich, Switzerland, approved the protocol for the study. Written informed consent was obtained from all parents and from children 14 years or older. All data were deidentified.

Study Procedures

Eligible patients with CAP were tested for the presence of *M pneumoniae* DNA in oropharyngeal swab samples by *M pneumoniae*-specific PCR.[9] Patients with mucocutaneous disease who had positive PCR results were tested with the *M pneumoniae*-specific IgM ASC ELISpot assay to confirm *M pneumoniae* infection, as described previously.[6] All children had a thorough clinical examination of the skin and mucous membranes. Patients with confirmed *M pneumoniae*-induced mucocutaneous disease were followed up for 6 months.

Statistical Analysis

Categorical and continuous variables were compared with the Fisher exact test and Mann-Whitney test, respectively. A case-control analysis was performed between patients with CAP and mucocutaneous disease who tested positive on the *M pneumoniae*-specific IgM ASC ELISpot assay and those without mucocutaneous manifestations. A 2-tailed $P < .05$ was considered to be statistically significant. Analyses were performed with R software, version 3.6.0 (R Foundation for Statistical Computing).

Results

Among 152 enrolled children with CAP (median [interquartile range] age, 5.7 [4.3-8.9] years; 84 [55.3%] male), 44 (28.9%) tested positive for *M pneumoniae* by PCR; of these, 10 children (22.7%) (median age, 8.7 years; range, 3.8-14.6 years; 6 [60%] male) developed mucocutaneous lesions (eFigure 1 in the Supplement). Diagnosis of *M pneumoniae* infection was confirmed in all 10 patients with mucocutaneous involvement by detection of *M pneumoniae*-specific IgM ASCs. In the 108 patients with CAP who tested negative for *M pneumoniae* by PCR, mucocutaneous disease (maculopapular skin eruptions and conjunctivitis) was observed in 3 (2.8%) ($P < .001$ compared with patients with CAP who tested positive by PCR).

Of the 44 patients with CAP who had positive *M pneumoniae* PCR results, 34 had peripheral blood mononuclear cells available for *M pneumoniae*-specific IgM ASC ELISpot assay testing and 31 tested positive. A case-control analysis of these 31 patients with CAP with positive *M pneumoniae*-specific IgM ASC ELISpot assay results found that the 10 patients with mucocutaneous disease had longer duration of prodromal fever (median, 10.5 days; interquartile range, 8.3-11.8 days; $P = .02$) and higher C-reactive protein levels (median, 31 mg/L; interquartile range, 22-59 mg/L [to convert to nanomoles per liter, multiply by 9.524]; $P = .04$) and were more likely to require oxygen (odds ratio, 17.6; 95% CI, 1.5-984.1; $P = .007$) compared with 21 patients without mucocutaneous manifestations (**Table 1**). Patients with mucocutaneous disease were more

Table 1. Comparison of Patients With *Mycoplasma pneumoniae*–Induced Mucocutaneous Disease and CAP Due to *M pneumoniae* Without Mucocutaneous Manifestation[a]

Characteristic	*M pneumoniae*–Induced Mucocutaneous Disease (n = 10)[b]	*M pneumoniae* CAP Without Mucocutaneous Manifestation (n = 21)	OR (95% CI)	*P* Value
Age, median (IQR), y	8.7 (6.0-12.2)	8.6 (6.7-11.0)	NA	.85
Male	6 (60)	11 (52)	1.4 (0.2-8.6)	>.99
Season at enrollment				
Spring (March-May)	3 (30)	3 (15)	2.5 (0.3-23.5)	.36
Summer (June-August)	3 (30)	7 (33)	0.9 (0.1-5.5)	>.99
Autumn (September-November)	2 (20)	7 (33)	0.5 (0.0-3.7)	.68
Winter (December-February)	2 (20)	4 (19)	1.1 (0.1-9.4)	>.99
Prior antibiotic treatment	7 (70)	9 (43)	4.4 (0.6-53.8)	.12
Preexisting disease	0 (0)	1 (5)	NA	>.99
Asthma or history of wheezing	0 (0)	1 (5)	NA	>.99
Pulmonary characteristics				
Prodrome, median (IQR), d				
Respiratory symptoms	10.5 (8.3-11.8)	9.0 (6.0-10.0)	NA	.17
Fever	10.5 (8.3-11.8)	7.0 (5.5-9.5)	NA	.02
Symptoms and signs[c]				
Temperature, median (IQR), °C	39.3 (38.7-39.9)	39.0 (39.0-39.5)	NA	.60
Runny nose	2 (20)	5 (24)	0.8 (0.1-6.4)	>.99
Sore throat	3 (30)	2 (10)	3.9 (0.4-55.6)	.30
Cough	10 (100)	19 (90)	NA	>.99
Chest pain	0 (0)	3 (14)	NA	.53
Wheezing	0 (0)	0 (0)	NA	>.99
Oxygen saturation <93%	5 (50)	1 (5)	17.6 (1.5-984.1)	.007
Oxygen supply, median (IQR), d	4.0 (2.0-6.0)	3.0	NA	.60
Dermatologic characteristics				
Prodrome, median (IQR), d	2.0 (1.5-2.0)	NA	NA	NA
Cutaneous involvement	9 (90)	NA	NA	NA
Mucosal involvement	5 (50)	NA	NA	NA
Oral	3	NA	NA	NA
Ocular	5	NA	NA	NA
Urogenital	2	NA	NA	NA
Anal	1	NA	NA	NA
Laboratory characteristics, median (IQR)				
WBC count, /μL	8800 (7000-10 800)	10 600 (7100-12 900)	NA	.60
Neutrophil count, /μL	6100 (4300-8700)	7800 (3800-10 400)	NA	.70
CRP level, mg/L	31 (22-59)	16 (7-23)	NA	.04
Treatment				
Antibiotics	8 (80)	20 (95)	0.2 (0.0-4.6)	.24
Corticosteroids	5 (50)	0 (0)	NA	.001
Clinical outcomes				
Hospitalization	7 (70)	4 (19)	9.0 (1.4-81.4)	.01
LOS, median (IQR), d	7.0 (4.5-9.0)	3.5 (2.5-4.0)	NA	.07
ICU admission	0 (0)	0 (0)	NA	NA
Long-term sequelae	3 (30)	0 (0)	NA	.03
Respiratory sequelae	2	NA	NA	NA
Dermatologic sequelae	1	NA	NA	NA

Abbreviations: CAP, community-acquired pneumonia; CRP, C-reactive protein; ICU, intensive care unit; IQR, interquartile range; LOS, length of hospital stay; NA, not applicable; OR, odds ratio; WBC, white blood cell.

SI conversion factors: to convert CRP values to nanomoles per liter, multiply by 9.524; to convert neutrophil and WBC counts to $\times 10^9$/L, multiply by 0.001.

[a] Data are presented as number (percentage) of study participants unless otherwise indicated. Differences between groups were determined by the Mann-Whitney test (medians) and Fisher exact test (proportions).

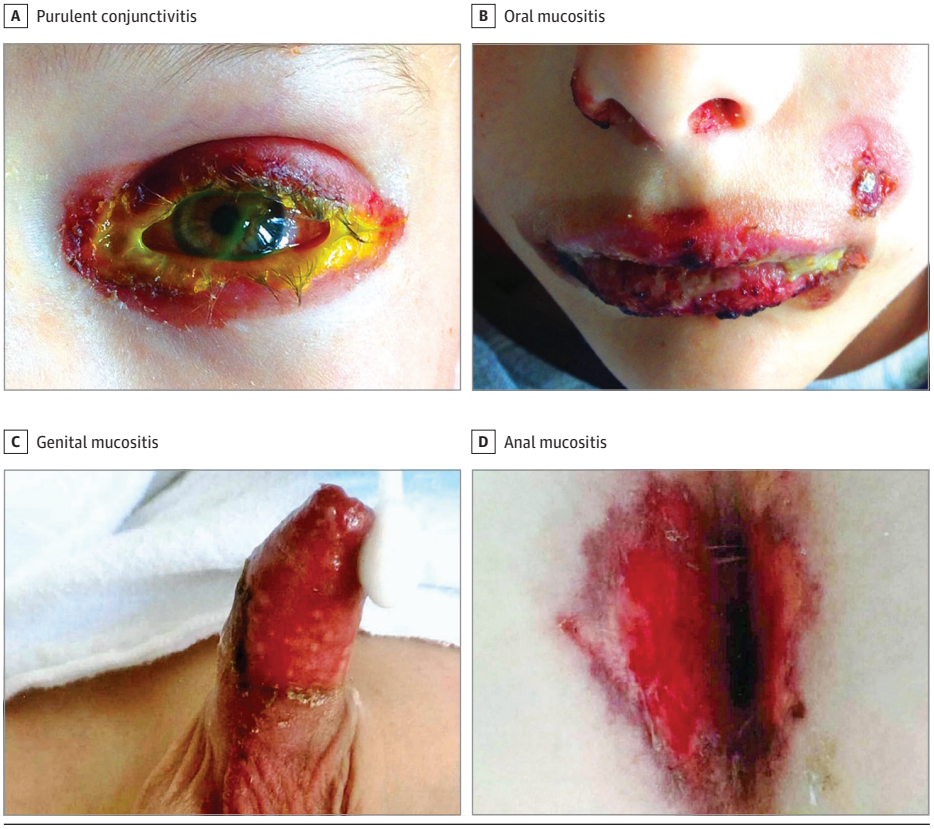
[b] Two patients with *M pneumoniae*–induced mucocutaneous disease were not included in the publication about the original cohort[6] because of incomplete specimens at inclusion.

[c] Inclusion criteria for CAP were presence of temperature higher than 38.5 °C and tachypnea, according to the British Thoracic Society guidelines.[8]

likely to be hospitalized (odds ratio, 9.0; 95% CI, 1.4-81.4; *P* = .01) and to develop long-term sequelae (3 [30%] vs 0; *P* = .03), including bronchiolitis obliterans, exertional dyspnea, and postinflammatory pigmentary alterations.

Among the 10 patients with *M pneumoniae*–induced mucocutaneous disease, 3 (6.8%) were diagnosed with MIRM, 2 (4.5%) with urticaria, and 5 (11.4%) with maculopapular skin eruptions (**Figure** and eFigures 2-4 in the Supplement). Detailed clinical characteristics of patients with *M pneumoniae*–induced mucocutaneous disease are given in **Table 2**. All patients with MIRM were hospitalized (median, 7.0 days; range, 5.0-13.0 days) and received antibiotics against *M pneumoniae* and a short course of systemic corticosteroids (methylprednisolone, 1-3 mg/kg, daily for 3 days). Mucocutaneous lesions

Figure. *Mycoplasma pneumoniae*–Induced Rash and Mucositis



healed without scarring, and postinflammatory pigmentary alterations were observed in 1 patient (eFigure 5 in the Supplement). No recurrences were observed during 6-month follow-up.

Discussion

To our knowledge, this is the first prospective longitudinal cohort study to examine *M pneumoniae*-induced mucocutaneous disease in children. We found that *M pneumoniae*-induced mucocutaneous disease occurred in 1 of 4 children with CAP who tested positive for *M pneumoniae* by PCR, including a considerable proportion (6.8%) with MIRM. *Mycoplasma pneumoniae* infection was confirmed in all patients with mucocutaneous involvement by the detection of specific IgM ASCs, which allows, in contrast to PCR and IgM serologic testing, the differentiation of *M pneumoniae* infection from carriage.[6]

Our study's observed frequency of *M pneumoniae*-induced mucocutaneous disease (22.7%) is in agreement with the estimates in the literature (25.0%-33.0%),[2-4] but MIRM occurred in our study more frequently (6.8% vs 1.0%-5.0%).[2] Although *M pneumoniae* may infrequently cause extensive blistering skin disease that is clinically indistinguishable from Stevens-Johnson syndrome and toxic epidermal necrolysis,[2] our data support the concept of MIRM as a specific entity.[3] A new proposed revised classification for severe cutaneous reactions in children suggests the term *reactive infectious mucocutaneous eruption*[10] to capture other pathogens that can also trigger a MIRM-like clinical presentation, such as *Chlamydophila pneumoniae*.[11] These case definitions are critical for patient management because early recognition of mucocutaneous disease as infection triggered rather than drug triggered (Stevens-Johnson syndrome and toxic epidermal necrolysis) enables more specific treatment and prognosis information and, most importantly, avoids restriction of possibly causative drugs.

The observation that *M pneumoniae*-induced mucocutaneous disease was associated with more pronounced inflammation is in agreement with a recent study about *M pneumoniae*-associated Stevens-Johnson syndrome[12] and suggests a distinct immune reaction. The rare detection of *M pneumoniae* from mucocutaneous lesions[3,4,13] further suggests an immune-mediated pathogenesis. Proposed immune mechanisms include immune complex-mediated vascular injury, cytotoxic T cell-mediated epithelial injury, or antibody-mediated disease.[2-4,14]

No evidence-based treatment guidelines exist for *M pneumoniae*-induced mucocutaneous disease. It remains unclear whether antibiotics and anti-inflammatory treatment, such as systemic corticosteroids or intravenous immunoglobulins, have any indication given the overall favorable disease course.[3,15] Nevertheless, patients require close monitoring to detect early signs suggestive of potential complications, such as bronchiolitis obliterans or mucosal sequelae.[2,3,12]

Table 2. Clinical Characteristics of *Mycoplasma pneumoniae*–Induced Mucocutaneous Disease

Characteristic	Case No.									
	1	2	3	4	5	6	7	8	9	10
Disease type	MIRM	MIRM	MIRM	Urticaria	Urticaria	Maculopapular skin eruptions	Maculopapular skin eruptions	Maculopapular skin eruptions	Maculopapular skin eruptions	Maculopapular skin eruptions
Prior antibiotic treatment (duration, d)	Clarithromycin (6)	Ciprofloxacin (2)	Amoxicillin-clavulanate (1)	NA	NA	Amoxicillin-clavulanate (2)	NA	Amoxicillin (1)	Amoxicillin (10)	Amoxicillin (5)
Pulmonary characteristics										
Prodrome: fever and RTI, d	10	11	8	9	14	8	11	7	12	13
Symptoms and signs										
Runny nose	No	No	No	No	No	Yes	Yes	No	No	No
Sore throat	Yes	No	Yes	No	No	Yes	No	No	No	No
Cough	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Oxygen saturation <93%	No	No	Yes	No	No	Yes	Yes	No	Yes	Yes
Oxygen supply, d	NA	NA	2	NA	NA	10	2	NA	6	4
Pulmonary infiltrate on chest radiograph	Yes	Yes	Yes	Yes	Yes	Yes	Yes	NA	Yes	Yes
Dermatologic characteristics										
Prodrome, d	2	4	2	(-6)[a]	0	(-5)[a]	2	2	2	0
Cutaneous involvement	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Acral	Yes	NA	No	No	No	No	No	Yes	No	No
Generalized	No	NA	No	Yes	Yes	Yes	Yes	No	Yes	No
Truncal	No	NA	Yes	No	No	No	No	No	No	Yes
Morphologic characteristics										
Vesiculobullous	No	NA	No	No	No	No	No	No	No	No
Targetoid	Yes	NA	Yes	No	No	No	No	No	No	No
Papules	No	NA	No	No	No	No	Yes	Yes	No	Yes
Macules	No	NA	No	No	No	Yes	Yes	Yes	Yes	Yes
Urticarial	No	NA	No	Yes	Yes	No	No	No	No	No
Mucosal involvement	Yes	Yes	Yes	No	Yes	No	No	Yes	No	No
Oral	Mucositis	Mucositis	Mucositis	NA	None	NA	NA	None	NA	NA
Ocular	Purulent bilateral conjunctivitis	Purulent bilateral conjunctivitis	Purulent bilateral conjunctivitis	NA	Nonpurulent bilateral conjunctivitis	NA	NA	Bilateral anterior uveitis[b]	NA	NA
Urogenital	None	Lesions of urethra and introitus	Lesions of glans, urethral meatus, penile shaft, and scrotum	NA	None	NA	NA	None	NA	NA
Anal	None	None	Perianal lesions	NA	None	NA	NA	None	NA	NA

(*continued*)

Table 2. Clinical Characteristics of *Mycoplasma pneumoniae*–Induced Mucocutaneous Disease (continued)

Characteristic	Case No. 1	2	3	4	5	6	7	8	9	10
Laboratory characteristics										
WBC count, /μL	16 100	62 000	10 800	6600	8600	8800	6900	11 700	9100	8700
Neutrophil count, /μL	13 280	3800	8700	5250	7390	6100	3860	9020	4280	5300
CRP level, mg/L	13	173	63	26	<4	46	36	72	24	21
Treatment (duration, d)										
Antibiotics	NA[c]	Doxycycline (7)	Clarithromycin (10)	Doxycycline (7)	Doxycycline (7)	Clarithromycin (7)	NA	Doxycycline (7)	Clarithromycin (7)	Doxycycline (7)
Systemic corticosteroids	Methylprednisolone (3)	Methylprednisolone (3)	Methylprednisolone (3)	NA	Prednisolone (5)	Prednisolone (3)	NA	NA[d]	NA	NA
Clinical outcome										
Hospitalization	Yes	Yes	Yes	No	No	Yes	Yes	No	Yes	Yes
LOS, d	5	7	13	NA	NA	11	2	NA	7	4
Reason	Severe mucositis	Severe mucositis	Severe mucositis, oxygen supply	NA	NA	Oxygen supply	Oxygen supply	NA	Oxygen supply	Oxygen supply
ICU admission	No	No	No	NA	NA	No	No	NA	No	No
Long-term sequelae	No	Yes	Yes	No	No	Yes	No	No	No	No
Respiratory sequelae	NA	Exertional dyspnea	None	NA	NA	Bronchiolitis obliterans	NA	NA	NA	NA
Dermatologic sequelae	NA	None	Postinflammatory pigmentary alteration	NA	NA	None	NA	NA	NA	NA
Time to full mucocutaneous recovery since onset, d	17	7	NA	4	34	7	4	22	2	4

Abbreviations: CRP, C-reactive protein; ICU, intensive care unit; LOS, length of hospital stay; MIRM, *Mycoplasma pneumoniae*–induced rash and mucositis; NA, not applicable; RTI, respiratory tract infection; WBC, white blood cell.

SI conversion factors: to convert CRP values to nanomoles per liter, multiply by 9.524; to convert neutrophils and WBCs to $\times 10^9$/L, multiply by 0.001.

[a] Days after enrollment.

[b] Anterior uveitis presented with bilateral conjunctival injection and eye pain for 2 days. An ophthalmologic examination revealed cells and flare in the anterior chamber. Apart from testing for *M pneumoniae*, a diagnostic workup was negative for antinuclear antibodies, rheumatoid factor, total immunoglobulins, and parvovirus B19.

[c] Already treated with an antibiotic against *M pneumoniae* before admission.

[d] Treatment consisted of topical corticosteroids in addition to a 1-week course of doxycycline. The uveitis resolved after 3 weeks of local treatment, and the visual acuity returned to baseline.

Limitations

This study may have a bias toward more severe disease because mild cases may not have been referred to our tertiary care center. We did not analyze *M pneumoniae* strains for genetic differences or test patients for other pathogens. Children younger than 3 years were excluded; therefore, the frequency and clinical presentation of *M pneumoniae*–induced mucocutaneous disease in children of that age are unknown. A significant proportion of children with maculopapular skin eruptions had prior amoxicillin (-clavulanate) treatment, making it difficult to differentiate infection- from drug-induced eruptions. However, the precise microbiological diagnosis of *M pneumoniae* infection together with the short period of drug exposure and the nonpruritic, faint presentation of eruptions in most of these cases favors an infectious cause.

Conclusions

In this study, mucocutaneous disease occurred significantly more frequently in children with CAP due to *M pneumoniae* than in children with CAP of other origins. *Mycoplasma pneumoniae*–induced mucocutaneous disease was associated with increased systemic inflammation, morbidity, and a higher risk of long-term sequelae. The overall prognosis of *M pneumoniae*–induced mucocutaneous disease was good. Further investigations are required to elucidate microbial or host characteristics that lead to this relevant and potentially severe extrapulmonary manifestation of *M pneumoniae* infection.

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Concept and design: Meyer Sauteur, Theiler, Berger.
Acquisition, analysis, or interpretation of data: All authors.
Drafting of the manuscript: Meyer Sauteur, Theiler.
Critical revision of the manuscript for important intellectual content: All authors.
Statistical analysis: Meyer Sauteur.
Obtained funding: Meyer Sauteur, Berger.
Administrative, technical, or material support: Meyer Sauteur, Weibel, Berger.
Supervision: Meyer Sauteur, Weibel, Berger.

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